

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1.-12. (cancelled)

13. (currently amended) An in vitro method for screening for candidate drugs for the treatment of Alzheimer's disease, said method comprising:

contacting slices of mouse hippocampal tissue containing cells, having a PS-1  $\Delta 9$  mutation and having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells to tetanic stimulation; and

determining the effect of said candidate drug on the synaptic potentiation of said mutant hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

14. (currently amended) An in vitro method for screening for candidate drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mammalian hippocampal cells comprising a PS-1  $\Delta 9$  presenilin gene mutation wherein said hippocampal cells have enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells to tetanic stimulation; and

determining the effect of said candidate drug on the synaptic potentiation of said mutant hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant

hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

15. (previously presented) The method according to Claim 14, wherein mouse hippocampal tissue slices comprise said mutant hippocampal cells.

16. (previously presented) The method according to Claim 14, wherein said enhanced synaptic potentiation is a result of a change in the GABA<sub>A</sub> receptor pathway.

17. (currently amended) An in vitro method for screening for candidate drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mammalian hippocampal cells comprising a PS-1 Δ9 presenilin gene mutation and having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to a tetanic stimulus;

measuring changes in potentiation with time of the mutant hippocampal cells and wild-type hippocampal cells and comparing the effect of said candidate drug on the synaptic potentiation of said mutant hippocampal cells as compared to the observed synaptic potentiation of said wild-type hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells as compared to the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

18.-19. (cancelled)

20. (currently amended) An in vitro method for screening for candidate drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mammalian hippocampal cells comprising a PS-1 Δ9 presenilin gene

mutation and having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to a tetanic stimulus at a first potential of glutamate currents and a second potential of GABA<sub>A</sub> currents;

measuring the synaptic response at each of the first and second potentials for said mutant hippocampal cells and said wild-type hippocampal cells and comparing the effect of said candidate drug on said mutant hippocampal cells and said wild-type hippocampal cells;

wherein a reduction in the enhanced synaptic response of the mutant hippocampal cells without a significant change in the synaptic response of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

21. (currently amended) An in vitro method for screening for candidate drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mouse hippocampal cells comprising a PS-1 Δ9 presenilin-1 gene mutation and having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells, with a candidate drug;

subjecting said mutant hippocampal cells and said wild-type hippocampal cells to tetanic stimulation; and

comparing the effect of said candidate drug on said mutant hippocampal cells and said wild-type hippocampal cells upon tetanic stimulation;

wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a significant change in the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

22.-25. (cancelled)

26. (previously presented) A method for screening for a candidate drug that suppresses intracellular calcium rise in slices of mouse hippocampal tissue containing cells having a PS-1  $\Delta 9$  mutation in a presenilin gene combined with a candidate drug for the treatment of Alzheimer's disease, said method comprising:

contacting hippocampal cells comprising a presenilin gene mutation and having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug that suppresses intracellular calcium rise in said cells; subjecting said mutant hippocampal cells to tetanic stimulation; and

determining the effect of said candidate drug on the ratio of peak inhibitory to excitatory responses;

wherein an enhanced said ratio of peak inhibitory to excitatory responses in said mutant hippocampal cells as compared to wild-type hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.